

Amendments to the Specification:

PLEASE NOTE: Some of the text is underlined in the original specification. In order to avoid confusion, additions are marked in double underline.

Please replace the paragraph at page 9, from line 17 through line 30, with the following paragraph:

-- The molecule may be a fusion polypeptide which comprises one or more amino acids interposed between the first and second parts which bind to cells, e.g. a fusion polypeptide which comprises a first amino acid sequence which can bind to an antigen bearing target and a second amino acid sequence which can bind to a leukocyte, and which further comprises at least one amino acid interposed between the first and second parts. The interposed amino acids may comprise, e.g., a linker sequence intended to lessen steric hindrance or other undesirable interactions between the aforementioned first and second parts. For, example, one such type of sequence takes the form  $(\text{Gly}_3\text{Ser})_n$ . Additional useful linkers include, but are not limited to  $(\text{Arg-Ala-Arg-Asp-Pro-Arg-Val-Pro-Val-Ala-Thr } \underline{\text{SEQ ID NO: 2}})_{1-5}$  (Xu et al., 1999, Proc. Natl. Acad. Sci. U.S.A. 96: 151-156),  $(\text{Gly-Ser})_n$  (Shao et al., 2000, Bioconjug. Chem. 11: 822-826),  $(\text{Thr-Ser-Pro})_n$  (Kroon et al., 2000, Eur. J. Biochem. 267: 6740-6752),  $(\text{Gly-Gly-Gly})_n$  (Kluczyk et al., 2000, Peptides 21: 1411-1420), and  $(\text{Glu-Lys})_n$  (Klyczyk et al., 2000, supra), wherein n is 1 to 15 (each of the preceding references is also incorporated herein by reference). In another embodiment, no amino acids are interposed between the first and second parts. --

Please replace the paragraph at page 91, from line 1 through line 7, with the following paragraph:

-- The IL21 receptor has been isolated by Parrish-Novak et al and found to be expressed by CD23 (+)B-cells, B-cell lines, a T-cell leukemia line, and NK-cell lines. The receptor gene has been mapped to human chromosome 16p12. The same receptor has been isolated by Ozaki et al, who called it NILR (novel interleukin receptor). The receptor (538 amino acids) is most closely related to human IL2 beta receptor. The receptor contains a WSXWS (SEQ ID NO: 3)

motif in the extracellular region, typical of type-1 cytokine receptors. The receptor is expressed on NK-cells, T-cells, and B-cell lines. --

Please replace the paragraph at page 136, from line 1 through line 15, with the following paragraph:

-- In one embodiment, the multifunctional molecule is a fusion polypeptide which comprises one or more amino acids interposed between the first and second parts which bind to cells, e.g. a fusion polypeptide which comprises a first amino acid sequence which can bind to an antigen bearing target and a second amino acid sequence which can bind to a leukocyte, and which further comprises at least one amino acid interposed between the first and second parts. The interposed amino acids may comprise, e.g., a linker sequence intended to lessen steric hindrance or other undesirable interactions between the aforementioned first and second parts. For, example, one such type of sequence takes the form  $(\text{Gly}_x\text{Ser})_n$ , wherein  $n$  is an integer from between 1 and 15, and  $x$  is an integer between 1 and 10. Additional useful linkers include, but are not limited to (Arg-Ala-Arg-Asp-Pro-Arg-Val-Pro-Val-Ala-Thr (SEQ ID NO: 2))<sub>1-5</sub> (Xu et al., 1999, Proc. Natl. Acad. Sci. U.S.A. 96: 151-156),  $(\text{Gly-Ser})_n$  (Shao et al., 2000, Bioconjug. Chem. 11: 822-826),  $(\text{Thr-Ser-Pro})_n$  (Kroon et al., 2000, Eur. J. Biochem. 267: 6740-6752),  $(\text{Gly-Gly-Gly})_n$  (Kluczyk et al., 2000, Peptides 21: 1411-1420), and  $(\text{Glu-Lys})_n$  (Kluczyk et al., 2000, supra), wherein  $n$  is 1 to 15 (each of the preceding references is also incorporated herein by reference). In another embodiment, no amino acids are interposed between the first and second parts. --

Please replace the paragraph at page 167, from line 1 through line 4, with the following paragraph:

-- GTX-5

5'pAATTCCGCGCCGGCACAGTGCTCAGAGACAAACTGGTCAAGTGTGAGGGCATCA  
GCCTGCTGGCTCAGAACACCTCGTGGCTGCTGCTGCTCCTGCTGTCCCTCTCCCTCCT  
CCAGGCCACGGATTTCATGTCCCTGTGACTGGGTAC3' (SEQ ID NO: 4) --

Please replace the paragraph at page 167, from line 12 through line 15, with the following paragraph:

-- GTX-6

5'pCCAGTCACAGGGACATGAAATCCGTGGCCTGGAGGAGGGAGAGGGACAGCAGG  
AGCAGCAGCAGCCACGAGGTGTTCTGAGCCAGCAGGCTGATGCCCTCACACTTGAC  
CAGTTTGTCTCTGAGCACTGTGCCGGCGCGG3' (SEQ ID NO: 5) --

Please replace the paragraph at page 168, from line 12 through line 20, with the following paragraph:

-- Upstream

5'CCGAATTCATGTGGCTGCAGAATTTACTTTTCCTGGGCATTGTGGTCTAC3'  
(SEQ ID NO: 6)

Downstream

5'CAGCCGGCTTTTTGGACTGGTTTTTTGCATTCAAAGGGGATATCAGTCAG3'  
(SEQ ID NO: 7) --

Please replace the paragraph at page 169, from line 11 through line 18, with the following paragraph:

-- The 280 bp GPI modification signal sequence from the yeast protein Gas1 was amplified by PCR from the yeast cosmid clone C9952 (ATCC). This PCR employed *pfu* polymerase and the primers:

Upstream Primer 5'GTAGCCGGCGCTAGCTCGGGGTCTTCTTCCAAGTCTA  
(SEQ ID NO: 8)

Downstream

Primer 5'TACGGTACCCCTAGGCCACAATGAAATAAGATACCATACC3'  
(SEQ ID NO: 9) --

Please replace the paragraph at page 170, from line 16 through line 19, with the following paragraph:

-- The GMCSF-Gas1 insert described above was amplified by PCR from pUC19-GMCSF-Gas1.1 using *pfu* polymerase and the primers:

Upstream 5'TACGGCCGGCACCCACCCGCTCACCC3' (SEQ ID NO: 10)

Downstream 5'TACGGCCGCCACAATGAAAATAAGATACCAT3' (SEQ ID NO: 11) --

Please replace the paragraph at page 178, from line 8 through line 13, with the following paragraph:

-- Human GM-CSF is amplified by PCR from a human T cell cDNA library (Clontech) using Pfu polymerase (Stratagene). The following primers are used:

Upstream

5'GCGAATCCCGGCCGGCACCCGCCCCGCTCGCCCAGCCCC (SEQ ID NO: 12)

Downstream

5'CAGCCGGCCTCCTGGACTGGCTCCCAGCAGTC (SEQ ID NO: 13) --

Please replace the paragraph at page 179, from line 11 through line 14, with the following paragraph:

--To clone GM-CSF GAS1g into the pITY-4 expression vector, PCR of this construct from the pUC19 vector is performed. The primers are:

5'TACGGCCGGCACCCGCCCCGCTCGCCCAGCCCC (SEQ ID NO: 14)

3'TACGGCCGCCACAATGAAAATAAGATACCAT (SEQ ID NO: 15) --

Please replace the paragraph at page 180, from line 9 through page 181 line 4, with the following paragraph:

-- pUC19 GM-CSF-K-HA was cloned starting with pUC19 GM-CSF-K-Gas1.1, which we produced in our laboratory. This plasmid includes a sequence that encodes murine GM-CSF fused to a downstream glycosylphosphatidylinositol modification sequence derived from the yeast GAS1 protein (the latter obtained from Dr. D. Wittrup, University of Illinois). A linker sequence is interposed between the GM-CSF and GAS1 portions. To insert the linker sequence, the plasmid pUC19 GMCSF-Gas1.1, also previously produced in our lab, was digested with NgoM IV and NheI. These restriction enzymes cut at the 3' end of the GM-CSF molecule and at the 5' end of the Gas1.1 sequence, respectively. The resulting plasmid was purified after electrophoresis through agarose gel using a kit manufactured by Qiagen. The following oligonucleotides were purchased :

5' CCGGCACTAGTGGCGGAGGGGGCTCCGGCGGCGGGGGCAGCG (SEQ ID NO: 16)

5' CTAGCGCTGCCCCCGCCGGCGCCCCCTCCGCCACTAGTG (SEQ ID NO: 17)

The synthetic oligonucleotides contain:

1. 5' overhang that anneals to NgoM IV digested plasmid DNA
2. 3' overhang that anneals to Nhe I digested plasmid DNA
3. DNA sequence coding for the peptide GGGGSGGGGS (SEQ ID NO: 18) where G stands for glycine and S stands for serine. This 10 amino acid sequence (G<sub>4</sub>S)<sub>2</sub> is designed to insert a kink/spacer in the protein between the GMCSF and the Gas1.1 moieties.
4. SpeI site to allow confirmation of cloning of the small fragment and for further manipulations. --

Please replace the paragraph at page 181, from line 18 through page 182 line 3, with the following paragraph:

-- pUC19 GM-CSF-K-Gas1.1. was digested with Nhe I and Kpn I. Nhe I cuts at the 5' end of the Gas1.1 coding sequence and Kpn I cuts at the 3' end of the Gas1.1 coding sequence,

respectively. The resulting plasmid with the GPI coding region removed, was purified after electrophoresis through agarose gel using a kit manufactured by Qiagen. The HA1 coding sequence was cloned by PCR from a plasmid encoding the HA gene of the A/PR/8/34 strain of influenza. The HA1 sequence used begins at amino acid 18, the start of the mature protein, i.e. lacking the secretion signal sequence. The 3' end corresponds to amino acid 344, eliminating the transmembrane region and substituting a termination codon. Primers for PCR of the HA1 sequence were as follows:

Upstream HA1 Primer

5' ATGCTAGCGACACAATATGTATAGGC (SEQ ID NO: 19)

Downstream HA1 Primer

5' ATGGTACCCGGCCGTTATCATCTGGATTGAATGGACGG (SEQ ID NO: 20) --

Please replace the paragraph at page 182, from line 19 through page 183 line 1, with the following paragraph:

-- PCR of pUC19 GM-CSF-K-HA was used to isolate a DNA fragment encoding GM-CSF-K-HA for cloning into a yeast expression vector. The PCR product contains Eag I cloning sites for in frame insertion into the yeast expression vector.

Upstream Primer

5' TACGGCCGGCACCCACCCGCTCACCC (SEQ ID NO: 21)

Downstream Primer

5' ATGGTACCCGGCCGTTATCATCTGGATTGAATGGACGG (SEQ ID NO: 22) --

Please replace the paragraph at page 185, from line 9 through line 16, with the following paragraph:

-- The HA-K sequence was first cloned by PCR of the HA1 coding sequence from a plasmid encoding the HA gene of the A/PR/8/34 strain of influenza.

Upstream Primer

5' CTGAATTCCGGCCGGACACAATATGTATAGGC (SEQ ID NO: 23)

Downstream Primer

5'  
ATGGTACCGCTGCCCCCGCCGGAGCCCCCTCCGCCACTTCTGGATTGAATGGAC  
GGAAT (SEQ ID NO: 24) --

Please replace the paragraph at page 186, from line 10 through line 14, with the following paragraph:

-- The GM-CSF fragment was cloned by PCR.

Upstream Primer

5' ACGGTACCGCACCCACCCGCTCACCCATC (SEQ ID NO: 25)

Downstream Primer

5' TAGGATCCCGGCCGTCATTTTGGACTGGTTTTTTGCACG (SEQ ID NO: 26) --

Please replace the paragraph at page 187, from line 10 through line 16, with the following paragraph:

-- PCR of pUC19 HA-K-GM-CSF was used to generate a DNA fragment encoding HA-K-GM-CSF for cloning into a yeast expression vector. The PCR product contains Eag I cloning sites for in-frame insertion into the yeast expression vector.

Upstream Primer

5' CTGAATTCCGGCCGGACACAATATGTATAGGC (SEQ ID NO: 27)



#### Downstream Primer

5' TAGGATCCCGGCCGTCATTTTTGGACTGGTTTTTTGCACG (SEQ ID NO: 28) --

Please replace the paragraph at page 192, from line 13 through line 25, with the following paragraph:

-- pUC19 human GM-CSF-K-HA (hGM-CSF-K-HA) is cloned starting with pUC19 GM-CSF-K-HA. pUC19 GM-CSF-K-HA. is digested with EcoRI and NgoM IV. EcoRI cuts at the 5' end of the murine GM-CSF coding sequence and Ngo M IV cuts at the 3' end of the murine GM-CSF molecule. The resulting plasmid with the murine GM-CSF coding region removed is purified after electrophoresis through agarose gel using a kit manufactured by Qiagen. The human GM-CSF coding segment is generated by PCR from a commercially available human cDNA library (Clontech). The human sequence begins at amino acid 18, the start of the mature protein, i.e. lacking the secretory signal sequence. The 3' end corresponds to amino acid 144, eliminating the endogenous termination codon.

#### Upstream hGM-CSF Primer

5' GCGAATTCCGGCCGGCACCCGCCCCGCTCGCCCAGC (SEQ ID NO: 29)

#### Downstream hGM-CSF Primer

5' TAGCCGGCCTCCTGGACTGGCTCCCAGCA (SEQ ID NO:30) --

Please replace the paragraph at page 193, from line 11 through line 19, with the following paragraph:

-- The pUC19 hGM-CSF-K-HA plasmid is purified according to the manufacturer's instructions using a kit purchased from Qiagen. PCR of pUC19 hGM-CSF-K-HA is used to generate a DNA fragment encoding hGM-CSF-K-HA for cloning into a yeast expression vector. The PCR product contains Eag I cloning sites for in frame insertion into the yeast expression vector.



Upstream Primer

5' GCGAATTCCGGCCGGCACCCGCCCCGCTCGCCCAGC (SEQ ID NO: 31)

Downstream Primer

5' ATGGTACCCGGCCGTTATCATCTGGATTGAATGGACGG (SEQ ID NO: 32) --